Remarks

Claims 1, 2, and 21-26 were pending; claim 1 is amended; claims 23-26 are canceled; and new claims 27 and 28 are added. As a result, claims 1, 2, 21, 22, 27, and 28 are pending. The amendment to claim 1 is supported, e.g., by paragraph [0046] and originally filed claims 14 and 15. Paragraph [0046] discloses expressing portions of the cDNA to make CA125 polypeptides, and using these CA125 protein portions, such as the amino terminal sequence, to make monoclonal antibodies. Originally filed claims 14 and 15 disclose fragments of SEQ ID NO:5 and antibodies that bind to SEQ ID NO:5 and fragments thereof. Claim 27 is supported, e.g., by SEQ ID NO:162 of parent provisional application serial no. 60/427,045, which is identical to residues 10,432-22,152 of SEQ ID NO:5. Claim 27 is also supported, e.g., by SEQ ID NOS:34, 36, and 38 in Tables 14, 16, and 18 of parent provisional patent application serial no. 60/299,380, which are disclosed to be the amino terminal domain, repeat domain, and carboxy terminal domain of CA125 and together make residues 10,432-22,152 of SEQ ID NO:5. Claim 28 is supported, e.g., by SEQ ID NO:310 of parent provisional patent application serial no. 60/427,045, which is identical to residues 1-10,431 of SEQ ID NO:5.

The Rejection of the Claims under 35 U.S.C. § 112, Second Paragraph

Claims 1, 2, 23, and 25 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection is respectfully traversed.

> The essential inquiry pertaining to this requirement is whether the claims set out and circumscribe a particular subject matter with a reasonable degree of clarity and particularity. Definiteness of claim language must be analyzed, not in a vacuum, but in light of: . . . The claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made.
>
> In reviewing a claim for compliance with 35 U.S.C. 112, second paragraph, the examiner must consider the claim as a whole to determine whether the claim apprises one of ordinary skill in the art of its scope and, therefore, serves the notice function required by 35 U.S.C. 112, second paragraph by providing clear warning to others as to what constitutes infringement of the patent. M.P.E.P. § 2173.02,

> citing *Solomon v. Kimberly-Clark Corp.*, 216 F.3d 1372, 1379, 55 USPQ2d 1279, 1283 (Fed. Cir. 2000).

Thus, the essential inquiry for determining compliance with 35 U.S.C. § 112, second paragraph, is whether one of ordinary skill in the art would understand the claims and would be apprised with a reasonable degree of clarity whether a particular embodiment infringes the claims or not.

The Examiner states that it is unclear how a nucleic acid is "adapted to express in a cell." There is nothing unclear about that. Obviously, the test for whether a nucleic acid is "adapted to express in a cell" is whether, when it is placed in an appropriate cell, it in fact does express the recited CA125 or fragment thereof in the cell. One of ordinary skill in the art would have no trouble determining the metes and bounds of the claims and whether a particular embodiment infringes the claims. He or she would simply test whether a nucleic acid in fact expresses CA125 or a fragment thereof in an appropriate cell.

The Examiner asks, "Are changes being made to the nucleic acid itself, i.e., SEQ ID NO:4 for adaptation? Is the insertion in the expression vector the adaptation? Is the nucleic acid sequence being chemically modified?" The Examiner is feigning ignorance. As the Examiner well knows, the requirements for expressing a nucleic acid are well known to a person of ordinary skill in the biotechnology arts.

Applicants have submitted with this response pages 322-323 of *Microbiology*, third edition, Prescott L.M. et al., 1996, Wm. C. Brown Publishers, Dubuque, Iowa. This introductory college textbook states:

> A cloned gene is not always expressed in the host cell without further modification of the recombinant vector. To be transcribed, the recombinant gene must have a promoter that is recognized by the host RNA polymerase. Translation of its mRNA depends on the presence of leader sequences and mRNA modifications that allow proper ribosome binding. These are quite different in eucaryotes and procaryotes, and a procaryotic leader must be provided to synthesize eucaryotic proteins in a bacterium. Finally, introns in eucaryotic genes must be removed because the procaryotic host will not excise them after transcription of mRNA; a eucaryotic protein is not functional without intron removal prior to translation.

> The problems of expressing recombinant genes in host cells are largely overcome with the help of special cloning vectors called expression vectors. (*Id.* at 322.)

As this introductory college textbook states, the requirements for expression are (1) a functioning promoter recognized by the host cell RNA polymerase to allow transcription of an mRNA, and (2) a leader sequence in the mRNA with a ribosome binding site to allow translation of the mRNA into protein. Expression vectors that have these elements are widely commercially available. For expression in procaryotic cells, introns must be removed, which is achieved by cloning a cDNA, such as SEQ ID NO:4. For expression in eucaryotic host cells, introns may be present.

If the Examiner's position is that one of ordinary skill in the biotechnology arts is not familiar with the elements necessary to express a recombinant nucleic acid in a host cell, Applicants respectfully request that he place that assertion in an affidavit, as is required under 37 C.F.R. § 1.104(d)(2).

A person of ordinary skill in the art is quite well aware of the elements necessary to express a nucleic acid in a host cell. He or she would have little doubt from looking at a design of a particular nucleic acid encoding CA125 (SEQ ID NO:5) or a fragment thereof, whether it is "adapted to express in a cell" the polypeptide. If there were any doubt, it would be a simple matter to test the nucleic acid construct to determine whether it in fact does express the polypeptide in a cell. Thus, one of ordinary skill in the art would have no trouble determining the metes and bounds of the claims and whether a particular embodiment infringes the claims. Thus, the notice function of 35 U.S.C. § 112, second paragraph is satisfied and the presently pending claims satisfy the definiteness requirement of 35 U.S.C. § 112, second paragraph. Accordingly, Applicants respectfully request withdrawal of the rejection of claims 1, 2, 23, and 25 under 35 U.S.C. § 112, second paragraph.

The Rejection of the Claims under 35 U.S.C. § 112, First Paragraph

Claims 1, 2, 23, and 25 were rejected under 35 U.S.C. § 112, first paragraph, on the basis that the specification allegedly does not contain a written description of the claimed invention. This rejection is respectfully traversed.

The Examiner stated as the reason for this rejection that the limitation of "adapted to express in a cell" has no clear support in the specification.

The Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, ¶1, "Written Description" Requirement, Fed. Register 66:1099-1111 (Written Description Guidelines) states, "While there is no *in haec verba* requirement, newly added claim limitations must be supported in the specification through express, implicit, or inherent disclosure" (Written Description Guidelines, at 1105).

The Examiner has the initial burden of presenting evidence or reasoning to explain why persons skilled in the art would not recognize in the original disclosure a description of the invention defined by the claims. (Written Description Guidelines, at 1107, citing *In re Wertheim*, 541 F.2d 257, 262, 191 USPQ 90, 96 (Ct. Customs and Patent Appeals 1976).

The Board of Patent Appeals and Interferences in *Ex parte Parks*, 30 U.S.P.Q.2d 1234 (Bd. Pat. App. & Int. 1994) stated:

> Adequate description under the first paragraph of 35 U.S.C. 112 does not require *literal* support for the claimed invention. . . . Rather, it is sufficient if the originally filed disclosure would have conveyed to one having ordinary skill in the art that an appellant had possession of the concept of what is claimed. (Emphasis added.)

Support for the concept of an isolated nucleic acid molecule encoding CA125 or a fragment thereof wherein the isolated nucleic acid molecule is an expression vector and is "adapted to express in a cell" CA125 or a fragment thereof is found throughout the originally filed specification and claims. Originally filed claim 20 recites, "A method to make a purified fragment of the CA125 polypeptide of SEQ ID NO: 5 comprising: (a) expressing a portion of the isolated nucleic acid molecule set out in SEQ ID NO: 4 to obtain a fragment of the CA125 molecule."

Paragraph [0008] states: "it is an object of the present invention to provide a recombinant CA125 cDNA molecule which can be introduced . . . to achieve transcription or expression of the cDNA. The utility of knowing the DNA sequence of a specific gene is that a recombinant protein can be produced."

Paragraph [0010] disclose "cloning vehicles" engineered to contain DNA sequences of the invention encoding CA125 or "portions of the sequence." Paragraph [0018] discloses use of "expression vectors" and cultured cells containing them.

Paragraph [0046] discloses expressing portions of the cDNA to make CA125 polypeptides, and using these CA125 protein portions to make monoclonal antibodies.

The words "adapted to express" do not appear in the specification. But there is no *in haec verba* requirement to satisfy the written description requirement. It is sufficient if the originally filed disclosure would have conveyed to one having ordinary skill in the art that an appellant had possession of the concept of what is claimed.

The specification provides abundant disclosure of expression vectors and expressing full-length recombinant CA125 (SEQ ID NO:5) and fragments thereof. Placing an nucleic acid in an expression vector to express polypeptides is clearly understood to entail a nucleic acid "adapted to express" the polypeptide. There can be no doubt that one of ordinary skill in the art upon reading the originally filed specification and claims, would understand that Applicants were clearly in possession of the concept of "An isolated nucleic acid molecule encoding CA125 (SEQ ID NO:5) or a fragment thereof; wherein the isolated nucleic acid molecule is an expression vector and is adapted to express in a cell CA125 (SEQ ID NO:5) or a fragment thereof; wherein the fragment thereof can be used to make monoclonal antibodies that specifically recognize CA125 (SEQ ID NO:5)." (Claim 1)

Accordingly, Applicants respectfully request withdrawal of the rejection of claims 1, 2, 23, and 25 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement.

The Rejection of the Claims Under 35 U.S.C. § 102

Claims 1, 23, and 25 were rejected under 35 U.S.C. 102(b) as being anticipated by Yin and Lloyd (*J. Biol. Chem.*, July 20, 2001, 276:27371-27375). This rejection is respectfully traversed.

The reference the Examiner cites is Yin and Lloyd (*J. Biol. Chem.*, July 20, 2001, 276:27371-27375). This states that the authors isolated a 5797-base pair sequence containing a stop codon but no clear 5' initiation sequence (abstract). And it is dated July

20, 2001. The alignment the Examiner shows is with Genbank locus AF361486, which is 21,112 bp (not 5797 bp) and states that it was updated on Sept. 8, 2003.

The present application claims priority to U.S. provisional patent application 60/427,045, filed November 15, 2002, before the update of genbank locus AF361486. U.S. provisional patent application 60/427,045 discloses all of SEQ ID NO:5. Table 21 of U.S. provisional application no. 60/427,045 discloses SEQ ID NO:162, which is the sequence of CA125 from residue 10,432 to residue 22,152 of SEQ ID NO:5 of the present application. And Table 25 of U.S. provisional application no. 60/427,045 provides SEQ ID NO:310, which is disclosed to be the amino terminal extension of CA125, residues 1-10,431 of SEQ ID NO:5 of the present application. Table 30 of U.S. provisional application no. 60/427,045 discloses the 66,764-nt cDNA matching SEQ ID NO:4 of the present application and encoding all of SEQ ID NO:5 . Accordingly, there is support for all of SEQ ID NO:5 in the present application before the publication date of Genbank locus AF361486.

The Yin and Lloyd *J. Biol. Chem.* paper does not disclose the sequence of the nucleic acid isolated. It states that the nucleic acid sequence they found produced a "deduced amino acid sequence of 1890 amino acids (Fig. 3)" (page 27372 second column) and it shows the deduced amino acid sequence in Fig. 3. Alignment of residues 1-100 of the sequence shown in the top portion of Fig. 3 of Yin and Lloyd with the present SEQ ID NO:5 shows imperfect homology with several sequences in the multiple repeat region from residues 12,070 to 21,868 of SEQ ID NO:5. The best homology begins with residue 13721 of SEQ ID NO:5.

Alignment of the sequence beginning with FNFWSS in the middle portion of Fig. 3 with SEQ ID NO:5 produced imperfect homology also with several segments of the multiple repeat domain of SEQ ID NO:5 between residues 12,070 and 21,868 of SEQ ID NO:5. The best homology begins at residue 15,004 of SEQ ID NO:5.

Alignment of the last line of sequence in Fig. 3, beginning with VLVDGYSPN with SEQ ID NO:5 produced alignment beginning at residues 22,076 of SEQ ID NO:5, in the carboxy terminal domain.

Thus, Yin and Lloyd does not disclose the actual sequence of nucleic acids that the authors discovered. The paper discloses that the nucleic acids encoded the protein

sequence shown in Fig. 3. This protein sequence is homologous with segments of the multiple repeat domain and carboxy terminal domain of CA125 (SEQ ID NO:5), which run from amino acid residues 12,070 to 22,152 of SEQ ID NO:5. No homology of the protein sequence disclosed in Fig. 3 of Yin and Lloyd is found with residues 1-10,431 of SEQ ID NO:5.

The sequence of residues 10,432 to 22,152 of SEQ ID NO:5 is disclosed in provisional patent application 60/299,380, to which the present application claims priority and which was filed June 19, 2001, before the publication date of Yin and Lloyd. This is the only portion of SEQ ID NO:5 with which Yin and Lloyd's sequence is homologous. U.S. provisional application no. 60/299,380 discloses that the CA125 molecule has an amino terminal domain shown as SEQ ID NO:34 in Table 14, a repeat domain shown as SEQ ID NO:36 in Table 16, and a carboxy terminal domain shown as SEQ ID NO:38 in Table 18. The carboxy end of the repeat domain of SEQ ID NO:36 overlaps with residues 1-154 of the carboxy terminal sequence shown in SEQ ID NO:38. Likewise, residues 1642-1797 of the amino terminal domain, SEQ ID NO:34, overlaps with the amino terminal of the repeat domain of SEQ ID NO:36. Thus, collectively, SEQ ID NOS:34, 36, and 38 of U.S. provisional application no. 60/299,380 disclose residues 10,432-22,152 of SEQ ID NO:5.

Since Yin and Lloyd (*J. Biol. Chem.*, July 20, 2001, 276:27371-27375) was published after the filing date of the parent U.S. provisional patent application serial no. 60/299,380 and discloses none of SEQ ID NO:5 not disclosed in provisional patent application serial no. 60/299,380, it does not anticipate the present claims. Likewise, accession number AF361486 was published after the filing date of parent provisional patent application serial no. 60/427,045 which discloses SEQ ID NO:5. Thus, neither Yin and Lloyd (*J. Biol. Chem.*, July 20, 2001, 276:27371-27375) nor Genbank accession number AF361486 anticipates the present claims. Accordingly, withdrawal of the rejection of claims 1, 23, and 25 under 35 U.S.C. § 102(b) over Yin and Lloyd (*J. Biol. Chem.*, July 20, 2001, 276:27371-27375) is respectfully requested.

Conclusion

Applicants believe the claims are in condition for allowance, and notification of allowance is respectfully requested. The Examiner is invited to telephone Applicant's attorney (651-207-8270) to facilitate prosecution of this application.

Respectfully submitted,

TIMOTHY O'BRIEN ET AL.

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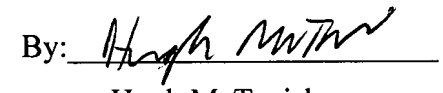
By: 
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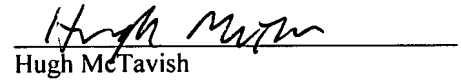
CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient first class postage, in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this day October 25, 2007.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